STUDIES IN THE SYNTHESIS OF SOME ARSENIC ANALOGS OF FLUORESCEIN

BY

HERBERT SAMUEL ELINS

B.S., Franklin and Marshall College, 1943
M.S., University of Illinois, 1947

AN ABSTRACT OF A THESIS

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN CHEMISTRY
IN THE GRADUATE COLLEGE OF THE
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R. UNIV. BIBLIOTHEEK LEIDEN

STUDIES IN THE SYNTHESIS OF SOME ARSENIC ANALOGS OF FLUORESCEIN

Introduction

The purpose of these researches was to study the synthesis of some arsenic analogs of fluorescein in which the carboxylic acid function is replaced by an acid arsenic moiety. The compounds sought were 6-hydroxy-9-(2-arsonophenyl)-3-isoxanthone and 6-hydroxy-9-(2-arsenosophenyl)-3-isoxanthone.

Apart from the synthetic interest, these compounds were desired because of a possible therapeutic utilization. Moore has recently shown that fluorescein itself is of value in the diagnostic differentiation of normal and malignant tissue in humans (1). Under controlled conditions this dye is selectively absorbed by certain neoplasms. By virtue of this property and because of its fluorescence under ultra-violet light Moore has been able to employ aqueous solutions of the sodium salt of fluorescein to confirm diagnosis in patients suspected of harboring malignancies and to outline the operative areas in the surgical treatment of brain tumors. Arsenic has long been of interest in the chemotherapy of malignant diseases.

Discussion Of Results

The synthesis of 6-hydroxy-9-(2-arsonophenyl)-3-isoxanthone and 6-hydroxy-9-(2-arsenosophenyl)-3-isoxanthone has been investigated. 6-Hydroxy-9-(2-aminophenyl)-3-isoxanthone was prepared by the condensation of methyl anthranilate and resorcinol in the presence of zinc chloride (2). Attempts to replace the amine function of this compound by the arsono group according to the method of Bart did not succeed. The product resulting from the inverted diazotization of the amine coupled with β-naphthol, but arsonation was not effected. The Scheller modification of the Bart reaction and the Sakellarios variation also failed to give any organic arsenic-containing material.

Synthesis of the desired arsono-compound by the Rosenmund arsonation of the analogous 6-hydroxy-9-(2-bromophenyl) 3-isoxanthone was not successful. The brominated isoxanthone was prepared by the condensation of *o*-bromobenzoic acid and resorcinol. When the Rosenmund reaction was applied to *o*-bromobenzaldehyde diethyl acetal only unchanged acetal was recovered.

The condensation of resorcinol with various *o*-arsenated benzoic acid derivatives — *e.g.*, *o*-carboxyphenylarsonic acid, methyl *o*-dichloroarsinobenzoate, and the internal anhydride of *o*-dichloroarsinobenzoic acid — yielded colored, fluorescent, arsenic-containing products that were not further characterized. The quantitative analyses could not be interpreted on the bases of the empirical formulas of the desired compounds or on those of any other compounds. These failures were probably due to the qualitative loss of arsenic under the reaction conditions. Evidence for this hypothesis is offered.

Methyl *o*-dichloroarsinobenzoate was prepared by the following route: *o*-arsonobenzoic acid, *o*-dichloroarsinobenzoic acid, *o*-dichloroarsinobenzoyl chloride, methyl *o*-dichloroarsinobenzoate. The hydrolysis of this product with cold aqueous sulfurous acid yielded methyl *o*-arsenosobenzoate.

When 2,4-dihydroxyphenylarsonic acid was reduced with sulfur dioxide in hydrochloric acid the carbon-arsenic bond was cleaved and resorcinol was isolated in good yield. The application of this reaction to 2,4-dimethoxyphenylarsonic acid yielded an oil that appeared to be the desired 2,4-dimethoxyphenyldichloroarsine. On distillation *in vacuo* the carbon-arsenic bond was severed and 1,3-dimethoxybenzene was recovered quantitatively. The lability of the arsenic moiety was not unexpected in the case of the arsenated resorcinol (3); however, its complete loss from the methoxylated benzene derivative was not anticipated.

Fluores*cin* diacetate has been synthesized by the reductive acetylation of fluorescein.

BIBLIOGRAPHY

1. Moore, Science, **106**, 130 (1947); *ibid.*, **107**, 569 (1948); Moore, Peyton, French, and Walker, J. Neurosurgery V., 4, 392 (1948).

2. Sen and Sircar, J. Indian Chem. Soc., **1**, 151 (1924-1925).

3. Banks and Hamilton, J. Am. Chem. Soc., **62**, 3142 (1940); Schmitz, Ber., **47**, 363 (1914).

VITA

The author was born at Lancaster, Pennsylvania on November 24, 1921. He attended the public schools of that city and was graduated from its J. P. McCaskey High School in June, 1939. In September of that year he matriculated at Franklin and Marshall College in Lancaster; in January, 1943, that institution granted him the degree of Bachelor of Science with Honors in Chemistry. From February, 1943, to February, 1946, he was on active duty with the United States Marine Corps. He entered the Graduate College of the University of Illinois in September, 1946, and was awarded the degree of Master of Science in June, 1947. He held a University Fellowship during the academic years 1947 to 1949.

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